(FILE 'HOME' ENTERED AT 15:24:44 ON 15 APR 2004)

FILE 'MEDLINE, CANCERLIT, EMBASE, BIOTECHDS, BIOSIS, CAPLUS' ENTERED AT 15:26:06 ON 15 APR 2004

L1	8623	S	FIV OR BIV OR CAEV OR MVV OR EIAV OR NON-PRIMATE LENTI?
L2	26752	S	TAT
L3	2598775	S	DELET? OR NON-FUNCTIONAL OR MUTA? OR ABSENT OR LACKING
L4	5465	S	L2 AND L3
L5	201	S	L4 AND L1
L6	66		DUP REM L5 (135 DUPLICATES REMOVED)

L6 ANSWER 38 OF 66 MEDLINE on STN DUPLICATE 23
AN 1998325200 MEDLINE
DN PubMed ID: 9658128
TI Priming with **tat-deleted** caprine arthritis encephalitis virus (**CAEV**) proviral DNA or live virus protects goats from challenge with pathogenic **CAEV**.
AU Harmache A; Vitu C; Guiguen F; Russo P; Bertoni G; Pepin M; Vigne R; Suzan M
CS INSERM U372, BP178, 13276 Marseille cedex 09, France.
SO Journal of virology, (1998 Aug) 72 (8) 6796-804.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 199808
ED Entered STN: 19980817
Last Updated on STN: 19980817
Entered Medline: 19980805
AB We previously reported that infection of goats with caprine arthritis encephalitis virus (**CAEV**) **tat**- proviral DNA or virus results in persistent infection, since the animals seroconverted and direct virus isolation from cultures of blood-derived macrophages was positive. In this study we wanted to determine whether goats injected with **CAEV tat**- proviral DNA or virus were protected against challenge with the pathogenic homologous virus and to investigate whether **CAEV tat**- was still pathogenic. All animals injected with **CAEV tat**- became infected as indicated by seroconversion and virus isolation. Challenge at 8 or 9 months postinfection demonstrated protection in four of four animals injected with **CAEV tat**- but did not in three of three mock-inoculated challenged goats. Challenge virus was undetectable in the blood macrophages of protected animals during a period of 6 or 10 months postchallenge. In two of four protected animals, however, we were able to detect the challenge wild-type virus by reverse transcriptase PCR on RNA directly extracted from synovial membrane cells surrounding the inoculation site. This result suggests that protection was achieved without complete sterilizing immunity. Animals injected with **CAEV tat**- and mock challenged developed inflammatory lesions in the joints, although these lesions were not as severe as those in **CAEV** wild-type-injected goats. These results confirm the dispensable role of **Tat** in **CAEV** replication in vivo for the establishment of infection and pathogenesis and demonstrate in another lentivirus infection model the efficacy of live attenuated viruses to induce resistance to superinfection.

L6 ANSWER 47 OF 66 MEDLINE on STN DUPLICATE 31
AN 95363954 MEDLINE
DN PubMed ID: 7636990
TI The caprine arthritis encephalitis virus **tat** gene is dispensable for efficient viral replication in vitro and in vivo.
AU Harmache A; Vitu C; Russo P; Bouyac M; Hieblot C; Peveri P; Vigne R; Suzan M
CS Institut National de la Sante et de la Recherche Medicale, U372, Marseille, France.
SO Journal of virology, (1995 Sep) 69 (9) 5445-54.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199509
ED Entered STN: 19950921
Last Updated on STN: 19970203
Entered Medline: 19950914
AB Caprine arthritis encephalitis virus (**CAEV**) is a lentivirus closely related to visna virus and more distantly to other lentiviruses, such as human immunodeficiency virus. The genomes of visna virus and **CAEV** contain a **tat** gene encoding a protein able to weakly transactivate its own long terminal repeat, suggesting that transactivation may be a dispensable function for viral replication. Three different **tat** gene **mutants** of an infectious molecular clone of **CAEV** were used to study their replication after transfection or infection of primary goat synovial membrane cells and of blood-derived mononuclear cells or macrophages. Our results showed no difference between replication of the wild type and either the complete **tat deletion mutant** or the **tat** stop point **mutant**, whereas slower growth kinetics and lower levels of expression of the partial **tat deletion mutant** that of the wild type were obtained in these cells. Quantitative PCR and reverse transcription-PCR analyses of the different steps of a single replicative cycle revealed an identical pattern of retrotranscription, transcription, and viral production, whereas time course analysis demonstrated that the intracellular level of viral genomic RNA was affected by the partial **tat deletion** at later time points. We then compared the infectious properties of the wild-type and **tat mutant** viruses in vivo by direct inoculation of proviral DNAs into the joints of goats. All the animals seroconverted between 27 and 70 days postinoculation. Moreover, we were able to isolate **tat mutant CAEV** from blood-derived macrophages that was still able to infect synovial membrane cells in vitro. This study clearly demonstrates that the **tat** gene of **CAEV** is dispensable for viral replication in vitro and in vivo.

L6 ANSWER 56 OF 66 MEDLINE on STN DUPLICATE 39
AN 93276539 MEDLINE
DN PubMed ID: 8389074
TI **Mutagenesis** of **EIAV TAT** reveals structural features essential for transcriptional activation and TAR element recognition.
AU Derse D; Newbold S H
CS Laboratory of Viral Carcinogenesis, NCI-Frederick Cancer Research and Development Center, Maryland 21702-1201.
SO Virology, (1993 Jun) 194 (2) 530-6.
Journal code: 0110674. ISSN: 0042-6822.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199306
ED Entered STN: 19930716
Last Updated on STN: 19970203
Entered Medline: 19930625
AB Certain members of the lentivirus subfamily of retroviruses encode unique transcriptional activator (**Tat**) proteins that modify the transcription complex after binding to the 5' end of nascent viral mRNA. The **Tat** proteins are modular, containing RNA-binding and activation domains that can be exchanged between different **Tat** proteins or replaced with heterologous protein fragments. While there is considerable sequence conservation among the divergent **Tat** proteins, there are also some structural differences that might be informative. For example, a cluster of basic amino acids in HIV-1 **Tat** is sufficient for RNA binding in vivo and in vitro. The homologous region of **EIAV Tat** is necessary but not sufficient for recognition of its cognate cis-acting RNA element; the entire C-terminal 26 amino acids of **EIAV Tat**, including the basic patch, are required. To better understand the structure-function relationships in **EIAV Tat**, we have generated a battery of expression plasmids encoding insertion, **deletion**, and missense **mutations** in the carboxy-terminal region of the **tat** gene. The plasmids were tested for their ability to trans-activate the **EIAV** promoter or to trans-inhibit a heterologous **Tat** protein. A **mutation** of a glutamine to an arginine in the cluster of basic residues generated a potent trans-dominant inhibitor of both **EIAV** and HIV-1 **Tat**, indicating that the **mutation** abolished RNA binding but did not alter the activation domain. **Mutations** at the extreme C-terminus of **EIAV Tat** impaired both RNA binding and activation domain functions, suggesting effects on secondary or tertiary structure.

L6 ANSWER 59 OF 66 MEDLINE on STN DUPLICATE 41
AN 91251194 MEDLINE
DN PubMed ID: 1645778
TI **Mutational** analysis of the equine infectious anemia virus **Tat**-responsive element.
AU Carvalho M; Derse D
CS Laboratory of Viral Carcinogenesis, National Cancer Institute, Frederick, Maryland 21702-1201.
SO Journal of virology, (1991 Jul) 65 (7) 3468-74.
Journal code: 0113724. ISSN: 0022-538X.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199107
ED Entered STN: 19910728
Last Updated on STN: 19910728
Entered Medline: 19910711
AB A hairpinlike structure is predicted to exist at the 5' end of equine infectious anemia virus (**EIAV**) RNA which is similar in many ways to the human immunodeficiency type 1 (HIV-1) **Tat**-responsive element (TAR). In **EIAV**, this structure has a shorter stem than in HIV-1 and lacks the uridine bulge. Primer extension analysis of **EIAV** RNA was used to identify the transcriptional start site in the viral long terminal repeat. Premature termination of primer elongation at the predicted double-stranded RNA region was frequently observed and suggests that the inferred hairpin structure exists under these conditions. We have functionally characterized **EIAV** TAR by site-directed **mutagenesis** and transient gene expression analysis. It is demonstrated here that the secondary structure of this element is essential for **Tat** action. **Mutations** that disrupted base pairing abolished TAR function, and compensatory **mutations** that restored the stem structure resulted in **Tat** activation. The TAR loop appears to be closed by two U.G base pairs that are likely to provide a unique structural motif recognized by the **Tat** protein. With one exception, substitutions of nucleotides within the **EIAV** loop sequence decreased TAR function. All nucleotide substitutions of the cytidine at position +14 increased **EIAV Tat** responsiveness; however, its **deletion** abolished trans activation. Our results lead us to propose that the **EIAV** and HIV-1 **Tat** systems employ closely related cis- and trans-acting components that probably act by the same mechanism.

L6 ANSWER 40 OF 66 MEDLINE on STN DUPLICATE 25
AN 1998354171 MEDLINE
DN PubMed ID: 9689746
TI Maedi-visna virus infection in sheep: a review.
AU Pepin M; Vitu C; Russo P; Mornex J F; Peterhans E
CS Unite pathologie des petits ruminants, Cneva Sophia-Antipolis, France.. vasa20@calva.net
SO Veterinary research, (1998 May-Aug) 29 (3-4) 341-67. Ref: 182
Journal code: 9309551. ISSN: 0928-4249.
CY France
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, ACADEMIC)
LA English
FS Priority Journals
EM 199809
ED Entered STN: 19980917
Last Updated on STN: 19980917
Entered Medline: 19980908
AB The maedi-visna virus (**MVV**) is classified as a lentivirus of the retroviridae family. The genome of **MVV** includes three genes: gag, which encodes for group-specific antigens; pol, which encodes for reverse transcriptase, integrase, RNAse H, protease and dUTPase and env, the gene encoding for the surface glycoprotein responsible for receptor binding and entry of the virus into its host cell. In addition, analogous to other lentiviruses, the genome contains genes for regulatory proteins, i.e. vif, rev and **tat**. The coding regions of the genome are flanked by long terminal repeats (LTR) which play a crucial role in the replication of the viral genome and provide binding sites for cellular transcription factors. The organs targeted by **MVV** are, in descending order of importance, the lungs, mammary glands, joints and the brain. In these organs, the virus replicates in mature macrophages and induces slowly progressing inflammatory lesions containing B and T lymphocytes. The clinical signs of **MVV** infection, i.e. dyspnea, loss of weight, mastitis and arthritis, are related to the location of these lesions. Infection with **MVV** induces the formation of antibodies which can be detected by agar gel immunodiffusion, ELISA and the serum neutralization assay. As neither antiviral treatment nor vaccination is available, diagnostic tests are the backbone of most of the schemes implemented to prevent the spread of **MVV**. However, since current serological assays are still **lacking** in sensitivity and specificity, molecular biological methods are being developed permitting the detection of virus in peripheral blood, milk and tissue samples. Future research will have to focus on both the development of new diagnostic tests and a better understanding of the pathogenesis of **MVV** infection.

L6 ANSWER 17 OF 66 MEDLINE on STN DUPLICATE 9
AN 2002408461 MEDLINE
DN PubMed ID: 12162812
TI Development of second- and third-generation bovine immunodeficiency virus-based gene transfer systems.
AU Matukonis Meghan; Li Mengtao; Molina Rene P; Paszkiet Brian; Kaleko Michael; Luo Tianci
CS Genetic Therapy, a Novartis Company, Gaithersburg, MD 20878, USA.
SO Human gene therapy, (2002 Jul 20) 13 (11) 1293-303.
Journal code: 9008950. ISSN: 1043-0342.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200302
ED Entered STN: 20020807
Last Updated on STN: 20030204
Entered Medline: 20030203
AB Lentivirus-based gene transfer systems have demonstrated their utility in mediating gene transfer to dividing and nondividing cells both in vitro and in vivo. An early-generation gene transfer system developed from bovine immunodeficiency virus (**BIV**) has been described (Berkowitz et al., J. Virol. 2001;75:3371-3382). In this paper, we describe the development of second-generation (three-plasmid) and third-generation (four-plasmid) **BIV**-based systems. All accessory genes (vif, vpw, vpy, and tmx) and the regulatory gene **tat** were **deleted** or largely truncated from the packaging construct. Furthermore, we split the packaging function into two constructs by expressing Rev in a separate plasmid. Together with our minimal **BIV** transfer vector construct and a vesicular stomatitis virus G glycoprotein-expressing plasmid, the **BIV** vectors were generated. The vectors produced by the three- and four-plasmid systems had titers greater than 1 x 10(6) transducing units per milliliter and were fully functional as indicated by their ability to efficiently transduce both dividing and nondividing cells. These results suggest that the accessory genes vif, vpw, vpy, and tmx are dispensable for functional **BIV** vector development. The modifications made to the packaging constructs improve the safety profile of the vector system. Finally, **BIV** vectors provide an alternative to human immunodeficiency virus-based gene transfer systems.

L6 ANSWER 62 OF 66 MEDLINE on STN DUPLICATE 44
AN 92074323 MEDLINE
DN PubMed ID: 1660215
TI Identification of conserved and variable regions in the envelope glycoprotein sequences of two feline immunodeficiency viruses isolated in Zurich, Switzerland.
AU Morikawa S; Lutz H; Aubert A; Bishop D H
CS NERC Institute of Virology and Environmental Microbiology, Oxford, U.K.
SO Virus research, (1991 Sep) 21 (1) 53-63.
Journal code: 8410979. ISSN: 0168-1702.
CY Netherlands
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199201
ED Entered STN: 19920124
Last Updated on STN: 19920124
Entered Medline: 19920109
AB The nucleotide sequences of the envelope (env) coding regions of two strains of the feline immunodeficiency virus isolated in Zurich, Switzerland (FIVZ1, FIVZ2) have been analysed. In addition, the complete sequence of the FIVZ1 isolate has been determined. Comparisons have been made with the previously published sequences of three North American isolates (PPR and the Petaluma strains FIV34TF10 and FIV14). The isolate FIVZ1 was very similar to the Petaluma strains of **FIV** and may represent a clonal derivative acquired by 'contamination'. Overall there are between 2.6% and 15.1% amino acid changes in the env gene products of the five isolates. Of the Zurich isolates, FIVZ2 exhibited the greatest divergence to the other viruses and based on its genotype, phenotype and origins probably represents a new isolate of **FIV**. Possibly the viruses diverged only recently from a common ancestor. Some 31 of the 33 cysteine residues and 17 of the 21 potential N-linked glycosylation sites of the FIV34TF10 env gene product were conserved among all five isolates. The open reading frame 3 (ORF3, or D) which overlaps the env gene (but is encoded in a different frame) has an ATG codon downstream of a potential splice acceptor site in all five isolates, supporting the view that it encodes a viral gene product. In ORF3 of FIVZ1 a stop codon was located 16 amino acids upstream of the stop codon of ORF3 of the other isolates. The ORF4 (or G) of isolate FIVZ2, thought to be the second coding exon of an **FIV** rev-like gene, contained a nucleotide **deletion** in amino acid 45 of ORF4, resulting in a--1 frameshift at this position. Comparison of the LTR sequences of the five isolates identified conserved promoter/enhancer elements. A potential stem-loop structure was identified in the R region of the LTRs of all the isolates, despite the heterogeneity of nucleotide sequences in that region. Such structures (TAR) are present in analogous regions of other lentiviruses and are responsible for **tat**-mediated trans-activatio

L6 ANSWER 52 OF 66 MEDLINE on STN DUPLICATE 35
AN 94162291 MEDLINE
DN PubMed ID: 8117736
TI An RNA-binding peptide from bovine immunodeficiency virus **Tat** protein recognizes an unusual RNA structure.
AU Chen L; Frankel A D
CS Department of Biochemistry and Biophysics, University of California, San Francisco 94141.
NC AI08591 (NIAID)
AI29135 (NIAID)
SO Biochemistry, (1994 Mar 8) 33 (9) 2708-15.
Journal code: 0370623. ISSN: 0006-2960.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals; AIDS
EM 199404
ED Entered STN: 19940412
Last Updated on STN: 19940412
Entered Medline: 19940407
AB The human immunodeficiency virus (HIV) **Tat** protein binds specifically to an RNA hairpin, TAR, located at the 5' end of its mRNA. **Tat** uses a single arginine residue within a short region of basic amino acids to recognize a bulge region in TAR. Here we show that a 17 amino acid arginine-rich peptide from the bovine immunodeficiency virus (**BIV**) **Tat** protein also binds to an RNA hairpin at the 5' end of its mRNA (**BIV** TAR), but recognizes different structural features of the RNA. **Mutagenesis**, RNase mapping, and chemical interference experiments indicate that bulge and stem regions of **BIV** TAR are recognized simultaneously by the **BIV** peptide and that the RNA adopts an unusual structure. **BIV Tat** binds to its TAR site with high affinity and specificity and, unlike HIV **Tat**, does not appear to use cellular proteins to stabilize RNA binding in vivo. Thus, two related viral activators have evolved rather distinct ways to recognize their RNA targets.

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L7	L6 same l3	24	L7
L6	L5 or l4	815	L6
L5	tat with deletion	157	L5
L4	tat with (deleted or non-functional or muta$ or absent or lacking)	760	L4
L3	L2 or l1	10162	L3
L2	FIV or BIV or CAEV or MVV or EIAV	10148	L2
L1	non-primate with lentivir$	48	L1

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L7: Entry 8 of 24 File: PGPB Aug 7, 2003

DOCUMENT-IDENTIFIER: US 20030147907 A1
TITLE: Retroviral vectors

Summary of Invention Paragraph:
[0018] It will be appreciated that the present invention provides a retroviral vector derived from a non-primate lentivirus genome (1) comprising a deleted gag gene wherein the deletion in gag removes one or more nucleotides downstream of nucleotide 350 of the gag coding sequence; (2) wherein one or more accessory genes are absent from the non-primate lentivirus genome; (3) wherein the non-primate lentivirus genome lacks the tat gene but includes the leader sequence between the end of the 5.zeta. LTR and the ATG of gag; and combinations of (1), (2) and (3). In a preferred embodiment the retroviral vector comprises all of features (1) and (2) and (3).

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L7: Entry 24 of 24 File: DWPI Aug 7, 2003

DERWENT-ACC-NO: 1999-418936
DERWENT-WEEK: 200358

TITLE: Retroviral vectors derived from a non-primate lentivirus genome

Basic Abstract Text (2):
DETAILED DESCRIPTION - Retroviral vectors derived from a non-primate lentivirus genome comprise a deleted gag gene. The deletion in gag removes one or more nucleotides downstream of nucleotide 350 of the gag coding sequence. One or more accessory genes are absent from the non-primate lentivirus genome or lack the tat gene but includes the leader sequences between the end of the 5' long terminal repeat (LTR) and the ATG of gag.

Equivalent Abstract Text (2):
DETAILED DESCRIPTION - Retroviral vectors derived from a non-primate lentivirus genome comprise a deleted gag gene. The deletion in gag removes one or more nucleotides downstream of nucleotide 350 of the gag coding sequence. One or more accessory genes are absent from the non-primate lentivirus genome or lack the tat gene but includes the leader sequences between the end of the 5' long terminal repeat (LTR) and the ATG of gag.

Equivalent Abstract Text (13):
DETAILED DESCRIPTION - Retroviral vectors derived from a non-primate lentivirus genome comprise a deleted gag gene. The deletion in gag removes one or more nucleotides downstream of nucleotide 350 of the gag coding sequence. One or more accessory genes are absent from the non-primate lentivirus genome or lack the tat gene but includes the leader sequences between the end of the 5' long terminal repeat (LTR) and the ATG of gag.

Equivalent Abstract Text (24):
DETAILED DESCRIPTION - Retroviral vectors derived from a non-primate lentivirus genome comprise a deleted gag gene. The deletion in gag removes one or more nucleotides downstream of nucleotide 350 of the gag coding sequence. One or more accessory genes are absent from the non-primate lentivirus genome or lack the tat gene but includes the leader sequences between the end of the 5' long terminal repeat (LTR) and the ATG of gag.

Equivalent Abstract Text (35):
DETAILED DESCRIPTION - Retroviral vectors derived from a non-primate lentivirus genome comprise a deleted gag gene. The deletion in gag removes one or more nucleotides downstream of nucleotide 350 of the gag coding sequence. One or more accessory genes are absent from the non-primate lentivirus genome or lack the tat gene but includes the leader sequences between the end of the 5' long terminal repeat (LTR) and the ATG of gag.